

Generation and Characterization of Aerosols and Vapors for Inhalation Experiments

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Control of aerosol and vapor characteristics that affect the toxicity of inhaled contaminants often determines the methods of generating exposure atmospheres. Generation methods for aerosols and vapors are presented. The characteristics of the resulting exposure atmosphere and the limitations of the various generation methods are discussed. Methods and instruments for measuring the airborne contaminant with respect to various characteristics are also described.

The toxicity of airborne materials is related to various characteristics of the material, the important ones being dependent on mechanisms and site of toxic reactions. Parameters of known importance include particle size, particle shape, chemical form, solubility, surface area and the presence of inert carrier particles. Regulation of the properties of interest often determines the method of producing the airborne contaminant and should determine the parameters to be measured in characterizing the exposure atmosphere.

Considerable research has been conducted on the effects of various characteristics of airborne particulate material on biological behavior. Several papers and books review this work, particularly in terms of deposition and clearance. (1-4) The parameters of primary interest in determining initial deposition in the respiratory tract are particle size and the particle size distribution of the aerosol (2). Particle parameters relating to deposition are inertia, sedimentation velocity, and diffusion rate (2). A particle's inertia and sedimentation rate depend on the same parameters (mass and aerodynamic drag) and are often defined in terms of gravitational sedimentation velocity. The parameter used is aerodynamic

diameter or the diameter of a unit density sphere that has the same terminal settling velocity as the particle of interest (1). For a spherical particle of diameter D and density ρ the aerodynamic diameter D_{AE} is given by eq. (1):

$$D_{AE} = D\sqrt{\rho C / \rho_0 C_{AE}} \quad (1)$$

where ρ_0 is unit density and C and C_{AE} are slip correction factors that apply when particle diameter is of the order of the mean free path of gas molecules. A given particle aerodynamic diameter will vary slightly with ambient conditions as mean free path varies with pressure and sedimentation rate varies slightly with temperature ($\sim 4\%$ variation from 22°C to 37°C). No conditions are specified for determination of aerodynamic diameter. Ambient conditions of interest should be used, as the kinetic behavior of the particles under these conditions is desired. Over the range of conditions encountered with inhalation exposures, these variations are slight. Biological variation and errors in sampling and particle size determination overshadow these effects. In addition, toxic effects are often related to total deposited mass, and most of the mass is normally associated with particles that are large enough to require minimal slip correction.

Figure 1 shows pulmonary deposition as a function of aerodynamic diameter for a breathing rate

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of 15 respirations/min and a tidal volume of 1450 cm³. The curve for $\rho = 1$ is taken from the Task Group on Lung Dynamics and was calculated by using a mathematical model of the lung (2). The pulmonary region refers to the nonciliated, functional portion of the respiratory tract.

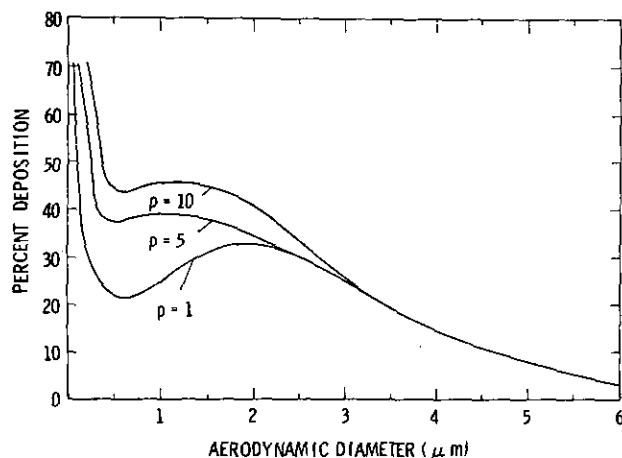


FIGURE 1. Pulmonary deposition as a function of aerodynamic diameter and particle density.

The use of aerodynamic diameter does not provide an estimate of diffusional deposition as diffusion is independent of particle density. If the exposure aerosol consists of small particles having densities greater than one, deposition will be greater than would be expected based on aerodynamic diameter (3). The increased deposition due to density has been estimated in Figure 1. This estimate was made by assuming deposition for particles larger than 1.0 μm with $\rho = 1$ is predominately by inertial mechanisms. This curve was then extrapolated to zero deposition for zero particle size. The real particle size was determined from the ratio of the square root of the densities ignoring the effect of slip factors. Diffusional collection was then determined from the difference between the total deposition curve and the extrapolated inertial deposition curve. Deposition due to diffusion was then added to inertial deposition at the aerodynamic diameter of interest to determine total deposition. No correction was made for decreased penetration to the pulmonary compartment due to increased deposition in tracheobronchial and nasopharyngeal regions. In the region of $0.1 \mu\text{m} < D_{AE} < 3 \mu\text{m}$ tracheobronchial deposition is almost constant (Fig. 2). However, deposition percentages for $\rho = 5$ and 10 are probably high. The curves do provide a representation of the effect of density on deposition.

In general, aerosols consist of particles of different sizes and must be described in terms of a size distribution. The log-normal distribution is frequently used as it provides a reasonable fit for aerosols produced by many methods. With this distribution the relative frequency of particles in the size interval $x \pm (dx/2)$ is given by eq. (2)

$$f(x) dx = \frac{1}{\sigma\sqrt{2\pi}} \exp \left\{ -\frac{(x - \mu)^2}{2\sigma^2} \right\} dx$$

where $x = \ln D$ and D is particle diameter, $\sigma = \ln \sigma_g$, σ_g being geometric standard deviation, CMD is count median diameter, and $\mu = \ln \text{CMD}$. Estimates of μ and σ_g are given by m and s , determined from samples of the aerosol. If the sample consists of N particles then

$$m = \frac{N \sum \ln D_i}{N} \quad (3)$$

and

$$s = \left[\sum_{i=1}^N (\ln D_i - \ln \text{CMD})^2 / (N-1) \right]^{1/2} \quad (4)$$

A distinct advantage of this distribution is that other properties of the aerosol described in terms of frequency with respect to diameter have the same σ_g with the median of the property related to CMD by the Hatch and Choate (5) equation [eq. (5)].

$$\ln D_r \approx \ln \text{CMD} + r(\ln \sigma_g)^2 \quad (5)$$

If $r = 2$, D_r is the median of the surface distribution; for $r = 3$, D_r is the median of the volume distribution. Characteristics of the log-normal distribution and descriptions of other distributions used to describe aerosols can be found in several books and papers. (3,5-8). Aerosols having small values of σ_g are said to be monodisperse. The limiting value of σ_g is arbitrary and in a practical sense dependent on the proposed use of the aerosol. Fuchs and Sutugin (9) have classified aerosols having $\sigma_g \leq 1.22$ as monodisperse.

The effect of size distribution on deposition is shown by Figure 2. This curve is from the Task Group on Lung Dynamics of the International Radiological Protection Commission (2). The envelopes represent the differences in deposition for log-normally distributed aerosols having σ_g values ranging from 1.20 to 4.50. The curve is for a breathing rate of 15 l/min at a tidal volume of 1450 cm³. Figures 1 and 2 illustrate the importance of particle size in determining the amount and location of deposited material.

Particle size is also important in determining clearance rate for relatively insoluble materials. Particles deposited in the upper portion of the

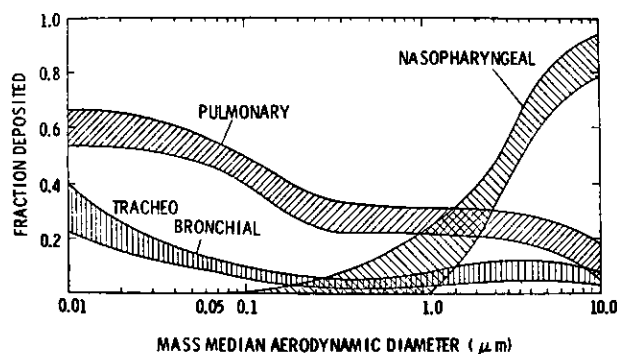


FIGURE 2. Respiratory tract deposition as a function of aerodynamic diameter and geometric standard deviation.

respiratory tract are rapidly cleared due to ciliary movement of the mucus layer lining the airways. Deposition probability in the upper respiratory tract is largely determined by aerodynamic diameter. Clearance from the pulmonary region of the respiratory tract is not completely understood and probably includes several mechanisms (1). Dissolution of particles has been suggested as one of the mechanisms (10), and this will depend on chemical form or solubility and on the total surface area of the deposited material. Surface-to-mass ratio is inversely proportional to particle size, so small particles will clear more rapidly by this mechanism. The parameter of importance in this case is the surface area distribution of the deposited particles.

The importance of different aerosol characteristics may dictate the collection of special types of samples. Special samples might be required of inhalation exposures carried out to determine mechanisms of toxicity or when extreme aerosols are being used (i.e., small dense particles). Reproducible exposures can be carried out only if a consistent method of determining particle size is used. If the results of the exposure indicate a need for additional information, the aerosol can be regenerated and characterized with respect to the parameters of interest. Aerodynamic diameter determination should usually be the first step because of its importance in deposition and clearance (2). Characterization should emphasize the distribution of "activity" or "active agent" with respect to aerodynamic diameter. Activity or active agent refers to the property or component of the aerosol particles that causes the effect to be studied. In the case of radioactive aerosols this would be radioactivity or for toxicity the chemical or toxic material of interest. If the aerosol is composed only of the toxic material or if the toxic material is homogeneously distributed in all particles, the activity distribution will be identical to

the mass distribution with respect to aerodynamic diameter. If the toxic material is adsorbed on the surface of inert particles, then the activity distribution will be the same as the surface distribution with respect to aerodynamic diameter. It is important to note that many diameters are used in defining aerosols. This is because specific effects are dependent on different parameters (as noted above) and also because different instruments measure different diameters.

Aerosol generation methods are normally classified according to the method of particle production. The categories of mechanical dispersion and vapor condensation cover most methods. Mechanical dispersion is commonly used as many types of these generators are commercially available. Aerosol generators used to disperse liquids include compressed air nebulizers, spinning disks, spray nozzles and ultrasonic nebulizers. Techniques for dispersing dry particles include air blast atomization, abrasion or grinding, and the use of fluidized beds.

Figure 3 is a schematic view of a compressed air nebulizer. Pressurized gas introduced behind the orifice passes into the nebulizer chamber expanding over the liquid feed tube. This decreases the pressure at the top of the feed tube. Liquid is drawn up the feed tube, entrained in the air-stream and drawn out into unstable filaments that break up due to capillary forces. Most drop-

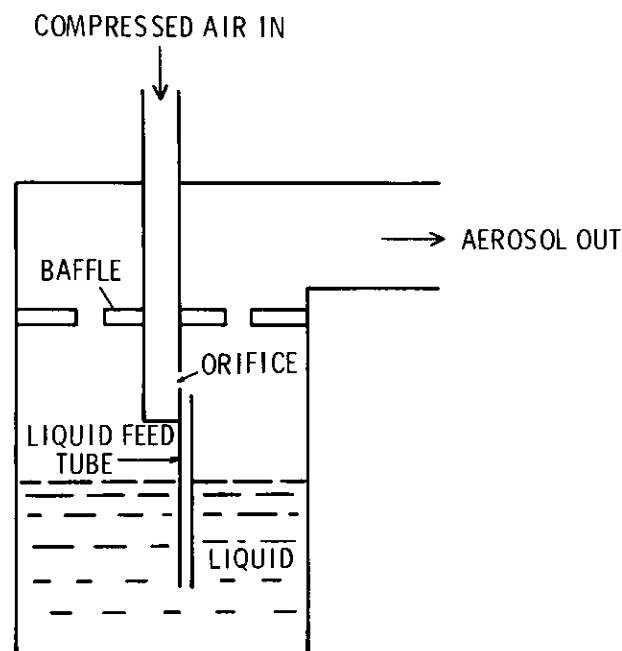


FIGURE 3. Schematic view of compressed air nebulizer.

lets impact on the walls of the atomization chamber or collide with larger droplets and return to the reservoir. A small fraction of the droplets (usually less than 1%) escape as useful aerosol. This fraction and the particle size range is determined to a great extent by the geometry of the atomization chamber and the flow rate through the generator. Many compressed air nebulizers incorporate baffles in the atomization chamber or exhaust ducting to limit the release of large particles. For these reasons, equations describing particle size produced by the atomization process are not very useful except as indicators of effects various parameters have on atomization. Mercer (3) has reported that the eq. (6) from Glukov (11) gives a reasonable estimate of the diameter of the droplet of average mass,

$$D_m = D_i A \left[1 + B \left(\frac{G_L}{G_G} \right)^m \right] \left(\frac{\rho_G V^2 D_i}{2\tau} \right)^{-0.45} \quad (6)$$

where A and B are functions of the dimensionless Suratman number (Su), where:

$$\text{Su} = \rho_L \tau D_i / \eta_L^2$$

D_i is the diameter of the liquid feed tube, V is the relative velocity between the gas and the liquid, G_L is the mass flow rate of liquid, G_G is the mass flow rate of gas, ρ_L is the liquid density, ρ_G is the gas density, η_L is the dynamic liquid viscosity, and τ is the surface tension between liquid and gas. Glukov reports (11) $A = 0.64$ when $\text{Su} > 400$, and experimental data indicates $B = 0.011$ and $m = 2$. The liquid parameters of viscosity and density appear in the dimensionless group (Suratman number) defining the valid range of the equation. The equation applies for most liquids of interest as $\text{Su} = 7 \times 10^3 D_i$ for water and $1.3 \times 10^5 D_i$ for ethyl alcohol. In this case, the equation indicates the liquid parameter most effecting particle size is surface tension. The output characteristics of some compressed air nebulizers are given in Table 1 (12-15). The Lauterbach, Dautrbande, and Lovelace nebulizers are laboratory devices that generally must be constructed and can be modified somewhat with respect to reservoir size and orifice diameter for specific applications. The other nebulizers are inhalation therapy devices and are available commercially or are similar to devices that are available. The orifice size of some of these nebulizers varies considerably between generators so the output in terms of microliters of solution generated as useful aerosol per minute will vary with flow rate. The specific out-

put (microliters of solution generated as useful aerosol per liter of jet gas) is largely a function of pressure for a wide range of orifice diameters so total output is directly proportional to flow rate at a given pressure (13). This effect can be used to increase the total output somewhat. Large increases in gas flow will cause large particles to be carried from the nebulizer significantly changing aerosol characteristics. The particle size range of the droplets produced by these nebulizers is fairly large with $\sigma_s \cong 2.0$. In general, if the particle size is small the specific output will be low. Particle size and output concentration in Table 1 are expressed in terms of the nebulized liquid. Dioctyl sebacate was used for the Collison nebulizer and water containing a small percentage of a salt or fluorescent dye was used for the other generators. Quite often the liquid is a solvent for the material of interest and exposure is to the particle remaining after the solvent evaporates. The equivalent volume diameter of the dry particle (real diameter if the dry particle is spherical or the diameter of a sphere having the same volume) can be determined from the solute concentration and droplet size by

$$KD_L^3 = \rho_D D_{EV}^3 \quad (7)$$

with

$$D_{EV} = (K/\rho_D)^{1/3} D_L \quad (8)$$

where D_{EV} is equivalent volume diameter, K is solute concentration (g/cm^3) ρ_D is dry particle density, and D_L is liquid drop diameter. Thus, particle size can be varied to some extent by varying concentration.

The total output of these nebulizers can also be increased by blowing auxiliary air through the atomization chamber (16). The specific output or output concentration is decreased. In most cases there is very little change in particle size. The specific output of compressed air nebulizers can be increased by placing a baffle very close to the orifice (17). The effect of the baffle location is shown in Figure 4 (13) for the Lovelace nebulizer using a 0-80 screw with a hemispherical end for a baffle. Optimum positioning of the baffle increased the output by a factor of five. The Retec nebulizer uses a fixed spherical baffle of plastic (15) and the Wright nebulizer (17) utilizes a flat plate for the baffle. Use of the baffle to increase specific output has little effect on particle size.

The gas used in the atomization process carries away solvent vapors causing solution concentration and resultant changes in aerosol character-

Table 1. Output characteristics of some compressed air nebulizers.

Nebulizer	Jet pressure, psi	Mass median diameter, μm	Geometric standard deviation	Specific output, μl solution/l. jet air	Output, μl solution/min ^a	Reference
Vaponefrin	12	5.6	1.80	~29	117	(12)
De Vilbiss #40	10	4.1	~1.85	16.0 ^b	155	(13)
De Vilbiss #40	20	3.2	~1.85	13.8 ^b	229	(13)
De Vilbiss #40	30	2.8	~1.85	12.8 ^b	270	(13)
Bennett Twin (2814)	7.5	6.8	1.80	23.8	119	(12)
Puritan (R6-051)	23	6.5	1.90	26.6	266	(12)
Lauterbach	10	3.8	~2.05	3.9	30 ^c	(13)
Lauterbach	20	2.4	~2.05	5.7	67 ^c	(13)
Lauterbach	30	2.4	~2.05	6.0	91	(13)
Dautrebande D-30	10	1.7	~1.65	1.42	21	(13)
Dautrebande D-30	20	1.4	~1.65	2.3	49	(13)
Dautrebande D-30	30	1.3	~1.65	2.4	65	(13)
Lovelace	10	—	—	15.3	14 ^d	(13)
Lovelace	20	5.4	1.90	30	39 ^d	(13)
Lovelace	30	—	—	35	58.3 ^d	(13)
Collison	15	—	—	8.7	53	(14)
Collison	25	1.9	2.5	6.7	55	(14)
Collison	30	—	—	5.8	55	(14)
Retec	20	5.7	1.8	35.2	208	(15)
Retec	30	3.6	2.0	35.9	284	(15)
Retec	50	3.2	2.2	31.9	376	(15)

^a Dioctyl sebacate is the nebulized liquid for the Collison, while water containing salt or a fluorescent dye is the nebulized liquid for the other nebulizers.

^b Zero auxiliary air flow.

^c Orifice diameter, 0.032 in.

^d Orifice diameter, 0.001 in.

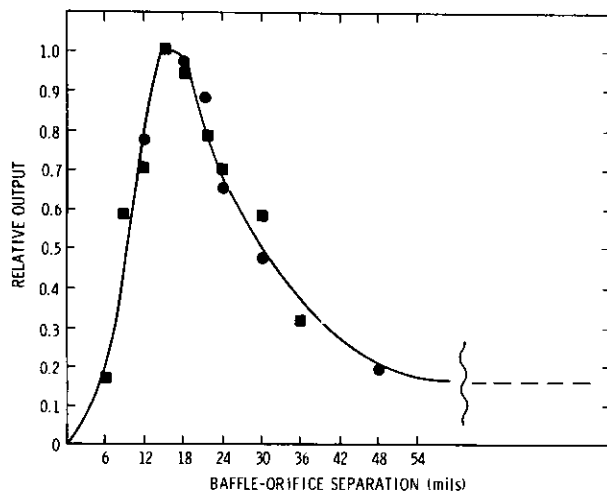


FIGURE 4. Effect of baffle position on output of compressed air nebulizer.

istics. The rate of concentration change is dependent on several factors. Liquid evaporation and gas expansion cool the nebulizer lowering the solvent vapor pressure. When operated with water, most nebulizers operate at about 10°C. Liquid evaporating from aerosol droplets leaving the generator will contribute to saturation of the gas

without increasing concentration in the reservoir. Thus, nebulizers with high specific outputs concentrate solution at a slower rate. A variety of methods have been used to minimize or eliminate this effect. These include humidification of the compressed air at room temperature (18) and at elevated temperature, (19) use of large separate reservoirs with recirculation pumps between the atomization chamber and reservoir, (20) controlled introduction of solvent to replace evaporation losses (18) and elimination of the reservoir with liquid supplied to the feed tube by a syringe pump (21). The best method is dictated by the solution being nebulized. If the material generated is expensive, radio-active, or very toxic, than large reservoirs or single pass systems cannot be used. If the solvent is very volatile, then a single pass system would be required.

Spray nozzles in which the liquid is forced through the orifice by connecting the jet to a pressurized reservoir (22) and spinning disks or cups (23,24) are used to produce droplets from liquids. These devices are commonly used in spray dryers, humidifying equipment and oil burners. In general, these devices produce large droplets with diameters of the order of hundreds of microns; thus, they are not used to produce aerosols of respirable size.

Vibrating piezoelectric crystals are also used for nebulization of liquids. A schematic view of an ultrasonic nebulizer is shown in Figure 5. The transducer is driven by an oscillator at frequencies ranging from 12 kHz to 3MHz. When the crystal oscillates with sufficient amplitude a fountain of liquid rises from the solution above the vibrating crystal. A jet of large droplets ($D \cong 1$ mm) forms at the top of the fountain. Capillary waves are generated on the surface of the fountain and the jet due to shock waves created by implosion of cavitation voids. (25) The wavelength λ of the capillary waves is given (26) by eq. (9):

$$\lambda = 8\pi\tau/\rho_L\omega^2 \quad (9)$$

where τ is surface tension, ρ_L is liquid density, and ω is frequency of the ultrasound. Experimental results reported by Lang (26) and Mercer, Goddard, and Flores (27) indicate that the count median diameter (CMD) of the ultrasonically produced aerosol is related to the capillary wavelength by

$$\text{CMD} = 0.34\lambda \quad (10)$$

where $\omega < 1$ MHz. At higher frequencies the particles are somewhat smaller than eq. (9) predicts (26).

The output characteristics of some ultrasonic nebulizers are given in Table 2. The total output of these generators is considerably higher than for compressed air nebulizers. The airflow through the atomization chamber can be controlled over a wide range of output concentrations. Coagulation is a problem with these generators because of the very high outputs and because the sound waves tend to concentrate particles at the

nodes (25). Preventing coagulation by dilution is the limiting factor on output concentrations. The ability to regulate particle size by varying the frequency of the crystal is also an advantage of these generators. The spread in particle size (σ_g) produced by these nebulizers is smaller than the spread produced by compressed air nebulizers. Most of the energy from the vibrating crystal is converted to thermal energy heating up the nebulizer so evaporation is a problem. Most of these nebulizers will evaporate at least 0.5 ml water/min (27).

Solid particles can be aerosolized from colloids or liquid suspensions of fine particles using the liquid nebulizers mentioned above. Use of these generators usually requires mechanical agitation of the solution to keep particles suspended. The particle size produced by the method is dependent on the size distribution of the suspended particles and on the size distribution of the nebulized droplets. This procedure has been used to produce particles containing encapsulated radionuclides by ion exchange of radionuclides with montmorillonite clay, nebulizing a colloidal suspension of the exchanged clay, then vitrifying the particles by passage through a heat column at approximately 1000°C (29,30).

Many devices have been designed for dispersing particles from dry powder. A schematic view of the Dustshaker designed by Deichman (31) is shown in Figure 6. The generator consists of a drum about 12 cm in diameter and about 20 cm high. A sieve containing dry powder is placed in top of the drum and the drum is shaken by a mechanical rapper. Dust particles settling down from the sieve are carried away by dry air blowing through the drum. In a similar device reported by Fuchs and Murashkevich (32), a

Table 2. Output characteristics of some ultrasonic nebulizers.

Nebulizer	Frequency, MHz	MMD, μm	σ_g	CMD, μm	0.34 λ , μm	Output, ml solution/min	Reference
Mist O ₂ Gen, 50-ml cup ^a	1.40	6.5	1.4	3.9	3.7	1.64	(27)
Mist O ₂ Gen, 10-ml cup ^a	1.40	6.5	1.5	4.0	3.7	0.88	(27)
De Vilbiss, gain setting 2 ^b	1.35	5.7	1.5	3.5	3.8	2.25	(27)
De Vilbiss, gain setting 3 ^b	1.35	6.9	1.6	3.5	3.8	3.83	(27)
De Vilbiss, gain setting 4 ^b	1.35	6.9	1.6	3.5	3.8	6.16	(27)
Denton-Swartz	1.00	—	—	5.2	4.6	~1.00	(28)
Denton-Swartz	3.00	—	—				

^a Mist O₂ Gen, model EN140, is available with two generation chambers: a 50-ml nebulizer cup with connections for an external reservoir and a 10-ml nebulizer cup.

^b De Vilbiss, model 880, has four gain settings for power to crystal.

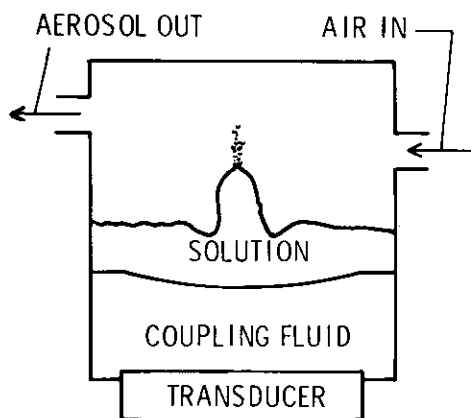


FIGURE 5. Schematic view of ultrasonic nebulizer.

pulsating airflow is used to sieve the powder. Airflow through the sieve is periodically reversed to clean the screen. Automatic filling hoppers are used to maintain a constant dust level in the sieve. The powder is deaggregated and dispersed with a spiral nozzle.

Aspirating devices utilizing the venturi pumping action of a jet to pick up dust are also used to aerosolize powders. Figure 7 shows a schematic view of an aspirator. Most of these devices also use the jet to break up and disperse the dust. This pickup process is size selective so various methods have been devised to expose the pickup tube to fresh powder. These have included rotating dust-filled tubes, (33) moving troughs (34), and fluidized beds (35). With most of these generators, considerable difficulty is encountered in maintaining a consistent output with respect to

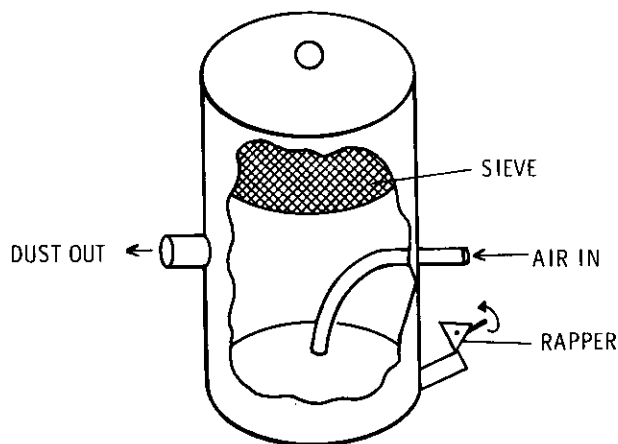


FIGURE 6. Schematic view of Deichman Dustshaker.

concentration and particle size. Pulsations in output can be dampened by passing the dust through a large volume holding tank before entering the exposure or experimental chamber. Willeke, Lo, and Whitby (36) used a fluidized bed consisting of metal spheres of about 100 μm diameter to dampen out fluctuations and break up aggregates from a dry powder aspirator.

The most successful devices for aerosolizing dry particles utilize mechanical abrasion of the surface of a compacted plug of powder. The plugs provide a consistent source of material as they are fed into the abrasion system mechanically. These devices can be quite simple. Dusts have been generated with spring-fed plugs and standard machine shop grinding wheels. The most successful devices use geared electric motor drives to feed the plug. The Wright dust feed mechanism (37) utilizes a scraper blade shown in Figure 8. Powder is compressed into a tube of slightly greater radius than the blade. The packed dust tube is rotated by a geared drive motor feeding the packed powder into the fixed scraper blade. Air is blown into the lower portion of the packed powder tube and passes through the air channel under the scraper blade sweeping particles into the hollow shaft supporting the blade. The flow rate is approximately $29 \times 10^3 \text{ cm}^3/\text{min}$. An impactor and outlet jet nozzle are incorporated to remove large particles and break up agglomerates.

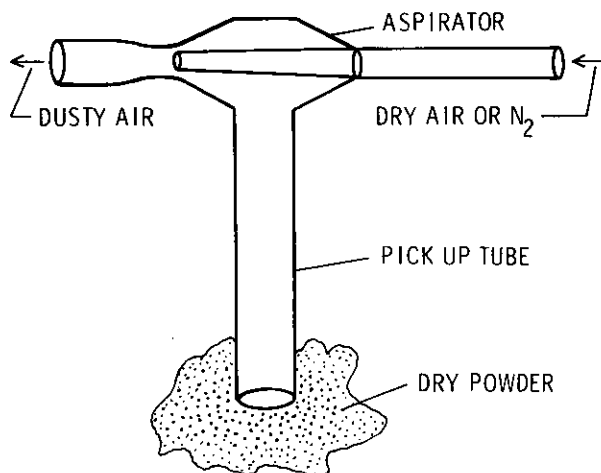


FIGURE 7. Schematic view of dust aspirator.

Two similar devices use air jets to abrade particles from the surface of plugs. The jet disperser of Dimmick (38) has been used to disperse powders and spores from a densely compacted

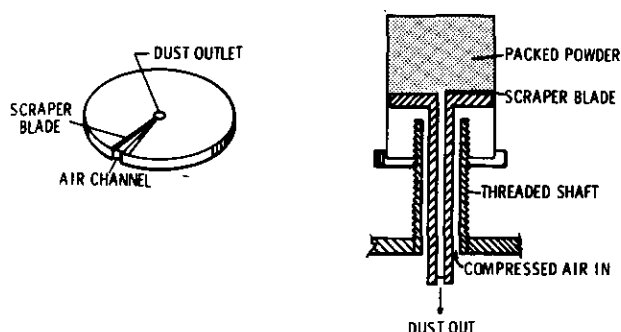


FIGURE 8. Schematic view of Wright dust feed scraper blade and dust tube.

plug and the "Konimiser" developed by Hounam (39) has been used to disperse lightly compacted plugs of asbestos fibers. Figure 9 shows a generator used to aerosolize fibrous glass and asbestos. This unit is a modified Timbrell type generator (40) developed by Ettinger et al. (41). The scraper blades in this generator operate at a higher speed than in the Wright dust feed and the plug is not packed as tightly.

The generation of aerosols by condensation of vapors is a straightforward process normally consisting of a heat source to vaporize the compound of interest, a gas to carry away the vapors and a cooling system for condensation of the vapors. Cooling is often accomplished by dilution with a cool gas to minimize coagulation. Condensation nuclei (very small particles relative to output aerosol) are often added to the dilution gas to enhance condensation (4). If condensation is carefully controlled the particles formed will be uniform in size.

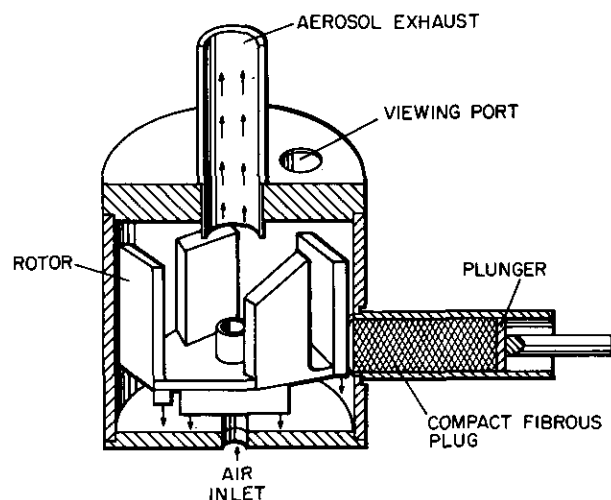


FIGURE 9. Schematic view of fibrous aerosol generator. (41)

The use of monodisperse aerosols can greatly simplify many studies. However, considerable problems are encountered in reproducibly generating monodisperse aerosols and in many cases useful concentrations can be produced only over a limited size range. The controlled condensation of substances having boiling points between 300 and 500°C has been used to produce monodisperse aerosols with the Sinclair-LeMer apparatus (42). A schematic view of this apparatus is given in Figure 10. Vapor is generated in the vaporizer and mixed with small condensation nuclei. The vapor and the nuclei are carried into the reheater. To insure complete evaporation of the aerosol material the reheater is maintained at a higher temperature than the vaporizer. Condensation and particle formation occurs in the chimney. Many forms of this generator have been built to provide more rapid thermal equilibration, (43) better regulation of temperature, and elimination of turbulence and streaming in the vaporizer region (44), and to provide more careful regulation of condensation nuclei (45-47). These generators produce particles ranging in size from $\sim 0.04 \mu\text{m}$ up to about $5 \mu\text{m}$ at concentrations from 10^4 to 10^7 particles/cm³. Substances that decompose with heat, have a wide range of boiling points or are impure cannot be generated in this manner. A variety of organics has been used (43-48). A high-temperature generator has been used to produce aerosols of zinc and cadmium (49).

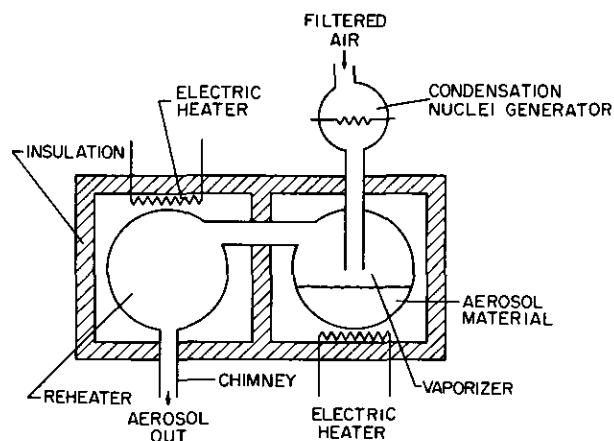


FIGURE 10. Schematic view of Sinclair-LaMer monodisperse aerosol generator.

Spinning disk generators have been used to produce monodisperse aerosols for deposition experiments (50). A simplified schematic view of a spinning disk is given in Figure 11. Various units

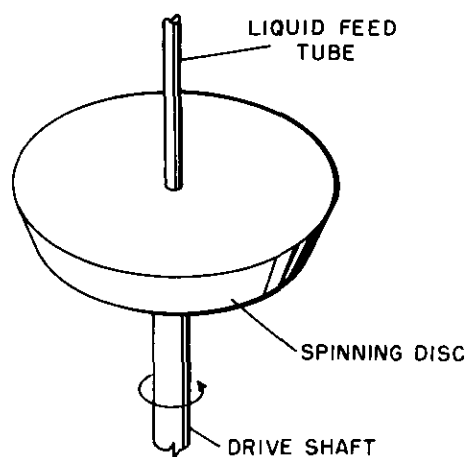


FIGURE 11. Schematic view of spinning disk aerosol generator.

have been built with disk diameters ranging from ca. 3 cm up to 8 cm. Electric and air motors have been used to drive these units at rotational speeds up to 70,000 rpm. (50-52) Liquid is fed on to the disk from a constant height reservoir or by a syringe pump. The liquid spreads out in a thin film that accumulates on the edge of the disk due to centrifugal force. When the force on a drop of liquid is sufficient to overcome capillary forces, a particle is thrown off the disk. As the droplet separates from the rim of the disk a small filament of liquid is drawn out and forms several satellite droplets that are much smaller than the primary droplet. The large differences in size are used to separate the particles by sweeping away the satellites with an airflow that is insufficient to overcome the inertia of the large particles. Another form of this generator is the spinning top (51, 53) having a disk with a conical bottom with turbine blades cut into the walls of the cone. Jets of air directed at the blades support the top and cause it to rotate. Spinning tops are normally smaller than spinning disks and operate at higher rotational speed. Spinning tops have been operated at rotational speeds of 150,000 rpm (53). These generators have been used to generate water droplets ranging in size from 10 μm up to several hundred micrometers. Considerable airflow is required to remove the satellites and to carry away and dry the primary particles so output concentrations are low.

Monodisperse aerosols have also been produced by forcing liquids out of capillary tubes or orifices while imposing regular mechanical vibrations on the orifice or capillary (54-58). The mechanical vibrations are normally imposed with piezoelectric crystals or electromechanical trans-

ducers driven by an electronic oscillator. The size of the droplets produced is determined by the size of the orifice, flow rate through the orifice and within some limits the frequency of vibration. (59) Orifices as small as 3 μm in diameter have been used to produce droplets of about 10 μm diameter (58). For normal operation, very small orifices are difficult to use as they frequently plug up. Larger orifices of 10 to 20 μm diameter can be used to produce small particles by dissolving the material of interest in a liquid solvent that evaporates from the droplets. Large airflows are required to carry away and dry the large droplets resulting in low output concentrations. These generators can be used to produce particles ranging in size from $\sim 0.5 \mu\text{m}$ up to several hundred micrometers in diameter at concentrations normally less than 10^3 particles/cm³. The aerosols produced are very monodisperse. They can be used for deposition studies and are excellent for instrument calibration. The low output concentrations limit the usefulness of these devices for biological effects studies.

Monodisperse aerosols have also been produced by electrical spraying (60-62) by passing liquids through a capillary with a high positive potential so the droplets formed on the end of the capillary are in an electric field. Droplets produced in this manner have very high electrical charges.

Aerosol sampling devices that separate particles according to size can be used to produce monodisperse aerosols of insoluble compounds. The instrument is used to separate and collect the particles. Particles of one size are then resuspended in a liquid and aerosolized with a nebulizer (63). A comprehensive review of methods for generating monodisperse aerosols have been written by Fuchs and Sutugin (9).

Some precautions are necessary to provide reproducible and consistent aerosols. To avoid changes in the solutions used in nebulizers and vapor condensation generators, it is often best to use an inert gas, such as nitrogen, in the generator. This can be mixed with other gases to change the chemical form of the particulate downstream from the generator and to provide a suitable exposure atmosphere. Aerosol particles produced by almost all methods (except vapor condensation) have electrical charges (64). These charges can lead to high and unpredictable losses in the exposure chamber and associated plumbing. High electrical charges may alter deposition distributions in the respiratory tract. Charge on aerosol particles can be reduced to equilibrium

distribution about zero by passing particles through a high-density atmosphere of bipolar ions produced by ionizing radiation (64-68) or through a field of ions produced by corona discharge (52,62). Aerosols to be used for inhalation experiments should be treated in this manner to reduce electrical charge and experimental variability. To eliminate electrical fields and subsequent particle losses in the exposure apparatus, the exposure chamber and associated particle conducting plumbing should be constructed of conductive material. This will eliminate the build-up of high static charges and electric fields. Hygroscopic aerosol particles exposed to a relative humidity above some critical value (69) will absorb water and grow to an equilibrium size (2). If the density of the dry particle is greater than one, particle density will decrease as water is absorbed. The ratio of aerodynamic diameter of the water solution droplet to the aerodynamic diameter of original droplet or dry particle is given (2) by eq. (11):

$$\frac{D_{AS}}{D_{AC}} = \left(\frac{q_s}{q_c} \right)^{1/6} \left(\frac{C_s}{C_c} \right)^{1/2} \left[1 + \frac{M_w}{M_c} \left(\frac{NH}{1-H} \right) \right]^{1/3} \quad (11)$$

where D_{AS} , D_{AC} are aerodynamic diameters of the solution droplet and the dry droplet, respectively; q_s , q_c are densities of the solution droplet and the dry droplet, respectively; M_w is the molecular weight of water; M_c is the molecular weight of the dry particle; N is the effective number of ions produced by dissolution of a solute molecule; and H is the relative humidity expressed as a fraction. It is apparent that the size of hygroscopic particles can vary with the humidity in the exposure chamber. These particles can also grow in the respiratory tract leading to a greater deposition than would be expected by measurements of aerodynamic diameter in the exposure chamber. The change in size can be very significant at high humidities. A 1 μm sulfuric acid droplet at 50% relative humidity (RH) will increase about 50% in aerodynamic diameter at 95% RH and ca. 300% at 99.5% RH.

Aerosols are normally characterized with respect to number or mass concentration and particle size distribution. The accuracy of these measurements can often be increased by taking separate samples for concentration and size measurements.

Mass concentration is often determined by collecting a filter sample at a known flow rate and analyzing for total mass of the toxicant of interest. A wide variety of filters are available that collect all sizes of particles very efficiently. A

comprehensive list of filters and associated equipment is available in the literature (70). The choice of filter is determined by the compound to be collected, the analytical method to be used and the desired flow rate. Filter samples can also be used to determine the solubility of toxic material associated with particles (71). Electrostatic precipitators are also used to collect total samples for concentration measurements. Most of these devices utilize a corona discharge to provide a unipolar ion field to charge particles for collection in an electric field. A schematic view of one configuration used for a sampling electrostatic precipitator is shown in Figure 12. Air is drawn through a concentric capacitor with a center electrode of fine wire with a sharp point. The voltage is set to provide a corona discharge from the point. The sample is collected on the outer tube which can be removed for sample analysis. A variety of these devices are available. A listing of electrostatic precipitators and operating characteristics can be found in Lippmann (70).

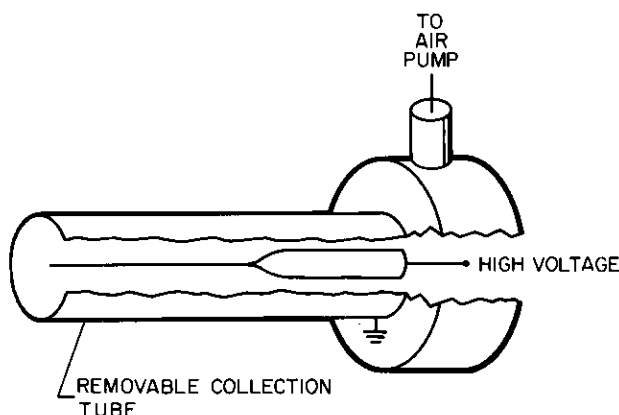


FIGURE 12. Schematic view of concentric electrostatic precipitator.

There are also direct reading devices that measure various concentrations or characteristics related to concentration. Many of these devices do not measure characteristics of interest in inhalation experiments. However, they can be used for monitoring the performance of inhalation chambers. These devices include light scattering photometers (70,72) that measure number concentration, integrating nephelometers (70,73) measuring total light-scattering cross section, beta gauges measuring mass in terms of beta ray adsorption (74,75) and piezoelectric crystal mass monitors measuring mass concentration associated with particles larger than some cutoff size (70,76).

Samples for particle size analysis are often collected for microscopic examination. Membrane filters can be used for this purpose as the filters can be cleared with immersion oil. Time-consuming techniques also exist for transferring samples from membrane filters to electron microscope grids (77,78). Precipitators are normally used to collect samples for examination by electron microscope. The point-to-plane electrostatic precipitator utilizes a corona discharge from a needle point to charge aerosol particles (70,79) for deposition on an electron microscope grid covered with a thin conductive carbon film. This device samples at flow rates of about 1 l./min. Figure 13 shows the cross section of an electrostatic precipitator that utilizes a radioactive tritium source to provide ions for charging particles (80). This unit operates at very low currents so high voltage can be supplied with a battery pack making the unit portable. This precipitator samples at low flow rates (5-10 cm³/min). Thermal precipitators are used to collect samples for both optical and electron microscopy (81,82). In thermal precipitators the aerosol enters a narrow channel with an electrically heated wire or ribbon on one side and a cool collection surface (electron microscope grid or glass coverslip) on the opposite side. Molecules striking the particle from the hot side have a higher velocity than molecules from the cool side so the particles migrate to the cool surface. These devices operate at low flow rates (5-10 cm³/min). Precipitators separate particles according to size to some extent, so care must be taken to insure that size measurements are made on a representative sample. The normal method is to measure particles completely across the trace in the direction of air flow.

A second type of instruments used for particle size analysis separate and collect particles according to aerodynamic diameter. Samplers of this type are very useful in inhalation experiments as they permit direct analysis of the toxic material with respect to aerodynamic diameter. One instrument of this type is the cascade impactor shown in Figure 14. Many types of this instrument have been built since May described the first one in 1945 (70,83-85). Figure 14 shows a cross-sectional view of the Mercer impactor (85). This instrument has seven stages, each with one round jet. The jet in successive stages has a smaller cross section so the air exits successive stages at higher velocities. The air is directed at an impaction plate where particles unable to negotiate the bend are collected. With increasing

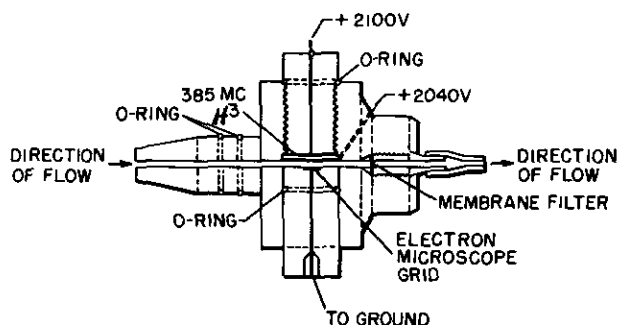


FIGURE 13. Electrostatic precipitator (80)

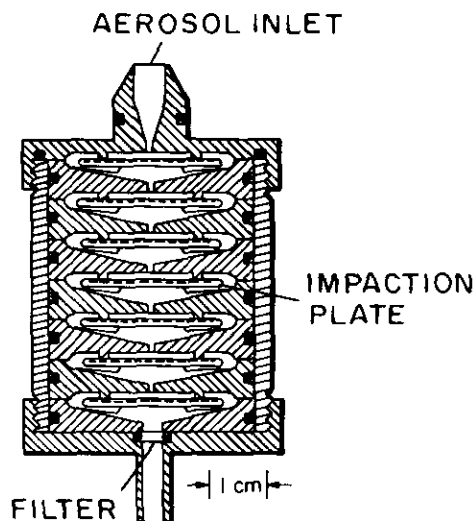


FIGURE 14. Seven-stage cascade impactor (85).

velocity at successive stages smaller particles are collected. The relatively simple construction of cascade impactors makes it possible to design instruments for specific sampling problems (3,86-88). Impactors have been developed to operate at flows ranging from a fraction of a liter per minute up to many cubic feet per minute. Particle collection occurs on a small area of the impaction plate. This can result in overloading of the collection surface with subsequent blow-off of material and changes in the operating parameters of the jet. This must be avoided by limiting the sample or changing the collection surface.

A variety of sampling instruments use centrifugal force to separate particles according to aerodynamic diameter (89-94). Figure 15 is a top view of a concentric channel centrifugal aerosol

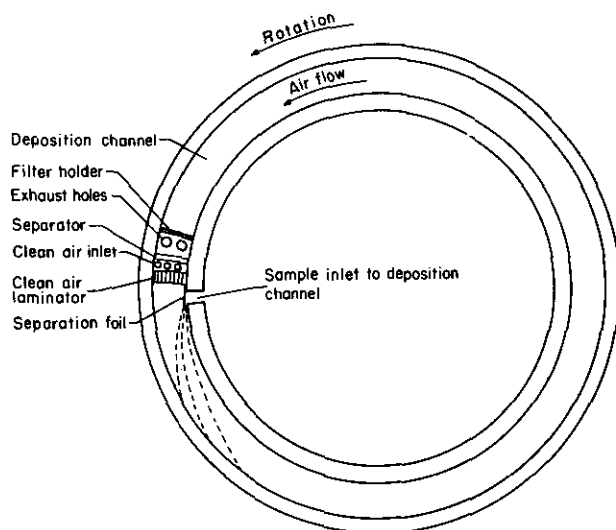


FIGURE 15. Deposition channel of concentric aerosol spectrometer (94).

spectrometer (94). The deposition channel is 3.3 cm deep and 1.1 cm wide. Particles enter the deposition channel in a thin layer next to the inner wall covered by a much thicker layer of clean air. Air is pulled down the channel by suction from behind the filter located at the end of the channel. The channel is rotating at high speed so particles are accelerated across the channel and deposit on the outer wall. A removable foil is placed on the outer wall for sample collection. Large particles are collected near the inlet and small particles penetrate to the filter. This type of instrument provides a continual separation of the particles according to aerodynamic diameter. The first device of this type, built by Stöber and Flachsbart (90), has a spiral channel approximately 180 cm long. These devices separate and collect particles as small as $0.06\ \mu\text{m}$ sampling at flow rates of from $100\ \text{cm}^3/\text{min}$ up to several liters per minute. The resolution of these instruments decreases with increasing sampling rate. Care must be taken in sampling aerosols with large particles as most of these instruments have size selective inlet losses (95).

There are several instruments that utilize light scattering measurements from single particles to size classify aerosols (96-98). In general, these devices measure only particles larger than $0.3\ \mu\text{m}$ in diameter. The laser-illuminated and laser-cavity devices may extend this range (97,99). Light scattering is not a simple function of particle size being dependent on particle shape and refractive index. If the light-scattering measurements are to be related to other characteristics

such as aerodynamic diameter, experimental calibrations must be carried out.

Inhalation hazard can also be assessed with two stage instruments that separate the aerosol sample into "respirable" and "nonrespirable" fractions. Most instruments of this type utilize an inertial collection device as a first stage to collect the "nonrespirable" fraction and a filter to collect the penetrating or respirable fraction (100-102). A discussion of these devices is given by Hatch and Gross (1).

Inhalation exposures of at least several days are usually required to produce detectable effects at low levels of chemical vapors in air. Therefore, vapor generation methods of greatest application are those capable of producing moderate flows for extended periods of time (103).

Among the batch methods of preparing controlled test atmospheres, the mixing and storage of contaminant-air mixtures in high-pressure cylinders best fits these requirements (104). The gas or liquid contaminants are first added to an evacuated cylinder by syringe injections, manometric measurements, or breakable glass ampoules containing weighed amounts of material. Next, filtered air is compressed into the cylinder to a selected pressure. Thorough mixing is essential. At high pressures this has been accomplished by heating and cooling opposite ends of a cylinder to enhance convection or by rolling it after adding steel spheres. This batch method is limited to volatile contaminants which are stable in the mixtures prepared. Cylinders can be refilled and replaced on a manifold to provide a continuous flow of prepared air. The mixture can be further diluted with another regulated stream of air to produce lower concentrations and higher humidities.

Mixing of streams of gases (105) is the simplest of the dynamic methods used to prepare known concentrations of vapors in air. Proportions of two or more gas streams are conveniently controlled with valves and measured with calibrated rotometers. For lower concentrations of vapors a gas blending device using automatic rotating stopcocks has been used (106).

Dynamic vapor generation methods involve the continuous addition of contaminant into a continuously flowing air stream. Effects of the walls of the system, though they may be high initially, are eliminated upon equilibrium. A variety of simple and ingenious techniques have been used to continuously introduce a contaminant vapor into an air stream. Physical properties, such as vapor pressure, diffusion rate, or permeation

rate, often are the basis for selection from among these. The more popular methods are: (1) injection of liquid onto a heated block by using a motorized syringe (105,107); (2) evaporation of a liquid or sublimation of a solid from a reservoir (103-108); (3) evaporation or sublimation followed by diffusion of vapor through a capillary (109); and (4) permeation of a vapor or liquid through a porous tube or water (110,111). Constancy of the air flow is important, and in the latter three cases precise temperature control is necessary.

A vapor inhalation exposure system must include a method for measuring or monitoring vapor concentration at the generation or mixing source and/or the breathing zone of the test animals (112). Such measurements provide warning of changes in the generation or test system. Selectivity of the monitoring technique is important when sampling in the breathing zone. Oxidation, hydrolysis, decomposition, or reaction products of the original vapors and animal vapors may also be present in the air taken from the test chamber. Immediately downstream of the vapor generation and mixing system less selectivity is required since the vapors present are known.

Instrumental methods of monitoring and identifying vapors are becoming more widely used (70,113,114). Three types of these are: continuous optical analyzers, continuous flame ionization analyzers, and intermittent gas chromatography analyzers. Optical analyzers measure absorption of light in a fixed wavelength range. The absorption may be in the near infrared region. Selection of such a monitor depends upon the optical spectra of gases and vapors present in the air sampled. Optical analyzers are sensitive to deposition on cell windows, which may become serious for compounds with low vapor pressures.

Continuous flame ionization analyzers respond rapidly to the total hydrocarbon content of the air sampled. They are, therefore, more useful for monitoring concentrations of hydrocarbons prior to the possible introduction of unknown vapors. Sensitivity and ease of operation are advantages of these instruments.

The gas chromatograph is the most versatile instrument for characterizing and measuring mixtures of vapors in air. It is highly specific and can measure many components of the air at one scan. Small, fully automated gas chromatographs are commercially available.

Sampling of gases and vapors can also be done intermittently using absorbing solutions or solid absorbents in tubes (115). These concentrate the sample for subsequent laboratory analysis by

wet-chemical or instrumental techniques. The selection of sampling device and analytical method will naturally depend upon which compounds are being monitored. However, the time lag for such sampling and analysis is often too long to adequately control the generator or chamber vapor concentrations.

In all sampling, care must be taken to insure that a representative sample is being collected. In exposure chambers having ports for exposing animals a similar port should be used for sampling at a rate similar to the average flow rate to the exposure port. In large immersion-type chambers, many samples must be collected across the exposure level to verify the existence or nonexistence of concentration gradients. In this case the sampler should be placed in the chamber to eliminate losses in sampling lines.

There are also cases where sampling must be carried out for particles and vapors. This must be done when exposure is to compounds with moderate vapor pressure or to compounds that will readily adsorb to inert particles. The latter process can also be used to alter the deposition distribution of vapors that are readily soluble in the mucus of the respiratory airways.

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